I. Scientific Abstract

This is a pilot trial to investigate the use of GM-CSF DNA as an adjuvant for peptide vaccination in patients with metastatic melanoma. The objective of this study is to determine the safety and adjuvant effect of vaccination with the gene coding for human GM-CSF with a multi-epitope melanoma peptide vaccine (tyrosinase and gp100 peptides) in patients with AJCC stage IIB, IIC, III and IV melanoma who are HLA-$A2^{+}$. We will assess whether use of GM-CSF DNA is safe and generates an immune response to peptides derived from antigens on melanoma cells.

In the Dose Ranging part of the study, cohorts of 3 patients will be treated at increasing dose levels of GM-CSF DNA delivered intradermally (100, 400, or 800 μg), followed by administration of both peptides to the same site on day 5. Patients will be treated monthly for three immunizations. During the first cycle, GM-CSF will be administered at two separate sites, the first site being used for subsequent peptide vaccination. The second site will be biopsied on day 5 to assess recruitment of dendritic cells. Pharmacokinetic studies will also be performed during the first cycle. Patients' peripheral blood mononuclear cells will be collected in order to measure the T cell responses induced by the vaccines. Toxicity will be assessed during this part of the study, although we do not expect to achieve a dose limiting toxicity (DLT). If we do not observe a dose-response for T cell responses and recruitment of dendritic cells, the dose for the second part of the study will be the maximum tolerated dose.

The second part of the study will assess the immunological efficacy of the vaccine. Nine patients will receive GM-CSF DNA delivered intradermally at one site, followed by administration of both peptides to the same site on day 5, every month for three immunizations. If patients with measurable disease have stable or clinically responding disease, additional vaccinations will be administered bimonthly for up to four additional vaccinations. A total of at least 18 patients is planned for both phases of the study. Patients' peripheral blood mononuclear cells will be collected in order to measure the T cell responses induced by the vaccines. Specifically, Elispot assays for $CD8^{+}$ T cells responses against the peptides will be assessed, and will be the primary method to determine the generation of a specific immune response to the peptide antigens.